

TUBERCULOSIS OF THE PROSTATE.

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(From the Pathological Laboratory of Rush Medical College.)

TUBERCULOSIS of the prostate has only recently become a subject of more than passing interest. Pathologists recognized the disease long ago and knew it to be not an infrequent condition, at least as a part of a more or less generalized genitourinary infection, but no adequate recognition of its clinical importance appears in the literature before 1892, when Marwedel² described four cases from Czerney's clinic and reviewed the subject in considerable detail. The earlier urologists looked upon it as a relatively rare and unimportant disease. Sir Henry Thompson in 1873 says that "the prostate is very rarely involved in tuberculous diseases, and is never affected alone or primarily." Socin in 1875 held a similar opinion as to its rarity, though he recognized a primary form. In a recent edition of his monograph (Socin and Burckhardt, 1902) more attention is given to the clinical importance of the subject, both in its primary and secondary aspects. Von Frisch and other recent monographists also refer to it as a disease of common occurrence and bring forward its clinical importance, though most text-books dealing more generally with genitourinary surgery fail to give it adequate recognition.

The following two cases of genitourinary tuberculosis³ originating in the prostate have recently been examined in the Pathological Laboratory of Rush Medical College and have seemed to me worthy of report. Finding very little bearing directly upon the subject in the American medical literature, I have deemed it worth while to review the subject at some length.

CASE I.—H. J., a Welshman, aged thirty-two years, and a salesman by occupation, was admitted to the Presbyterian Hospital, Chicago, January 20, 1903, to the service of Dr. Billings. An uncle on the paternal side died of tuberculosis; otherwise the family history is negative. He has had the usual diseases of childhood, but no serious illness since.

He has been an habitual and heavy indulger in alcoholics, especially during the last four years. Recently while receiving treatment

¹ An alphabetical list of authors quoted will be found at the end of this article.

² The records of these cases were put into practically the form in which they now appear by Dr. Epley, who as a student at Rush began their preparation for publication. Upon his graduation he left the city to engage in practice and the cases fell into my hands. I take this opportunity of expressing my indebtedness to Dr. Epley for the work which he had completed.

for alcoholism, he had a severe diarrhoea lasting two weeks, during which he passed a good deal of mucus accompanied by colic and tenesmus. These have entirely disappeared at the present time. He states, however, that for the last five years there have been occasional attacks of pain and diarrhoea. There is a history of two attacks of acute gonorrhoea, the last of which occurred eighteen months ago, and has continued to the present time as a slight urethral discharge, with pain on urination.

On admission the patient states that on December 22d he had a chill of moderate severity followed by a temperature of 104° , and was compelled to remain in bed. There was a severe dry cough, without expectoration, and great loss of strength. He has vomited five times in the last two weeks, and on the morning of admission he vomited a small quantity of bloody material. He complains of great weakness and dizziness upon standing or stooping over; upon exertion there is precordial pain, moderate dyspnoea, and palpitation of the heart. Urination is frequent and painful.

On physical examination the head and neck are found to be normal, the tongue red and raw-looking. Heart's apex in the fourth interspace in the nipple line, with the left border of dulness one-half inch to the left of this. A systolic murmur is heard in the mitral area and transmitted to the left axillary region. A few rales are heard over each lung; these appear and disappear and change place from time to time. Liver enlarged, tender, and extends three fingers' breadth below the costal margin, its edge hard and smooth. Rectal examination shows small hemorrhoids. The prostate is slightly enlarged and tender; upon massaging the gland a thin, purulent fluid escapes from the meatus, smears of which show by ordinary staining a few bacilli, numerous streptococci, and a few gonococci. The extremities are normal.

On admission the patient's temperature was 100° , pulse 112, respiration 20. There were trivial variations in these up to February 7th, when a temperature of 104.6° was registered after injecting 3 mg. of tuberculin. Subsequent to this the fever was irregular, often registering 103° and tending to remain high. On March 2d the patient had a pronounced chill, followed by a subnormal temperature, which lasted until the following afternoon, when he died.

Slight jaundice and a palpable spleen were noted on February 1st. On January 21st, the day after admission, the blood count was: erythrocytes, 2,448,000; leukocytes, 8000; hæmoglobin, 70 per cent. A month later erythrocytes and hæmoglobin were practically the same, the leukocytes having fallen to 1040. Examination of the feces, January 25th, gave a negative result. Sputum examinations on two occasions failed to show tubercle bacilli. The urine on various occasions showed a small amount of albumin and much pus. No casts were present. Search for tubercle bacilli in the sediment was made on several occasions, with negative result.

A clinical diagnosis of tuberculosis involving the lungs and genito-urinary tract was made. This was confirmed by the reaction to tuberculin, after which there was evidently rapid dissemination.

Autopsy. The following anatomical diagnosis was made at the post-mortem by Dr. Bassoe: Caseous tuberculosis of the prostate, bladder, right kidney, seminal vesicles, epididymes, periaortic lymph glands, and left lung; acute miliary tuberculosis of the lungs, spleen, and liver; acute splenitis; chronic parenchymatous nephritis; parenchymatous and fatty degeneration, with cirrhosis of the liver; bilateral fibrous pleuritis; fibrous perisplenitis; sclerosis of the aorta and coronary arteries; chronic gastritis; follicular duodenitis.

Only the more important findings are repeated in detail.

The left lung has a universally thickened pleura, especially marked at the apex. On section a few minute grayish nodules are found scattered throughout. At the middle of the lower lobe, near the surface, is a cavity, 1 cm. in diameter, containing a purulent material. Minute grayish nodules lie about it, and there are a few small caseous areas. The right lung contains numerous miliary and submiliary tubercles, but no caseous focus is discovered.

The right kidney contains numerous grayish necrotic areas in the medullary portion. The larger of these measure up to 3 cm. in diameter, are partially excavated, and communicate with the pelvis of the organ. The cortex represents only a few pinhead-sized nodules. The mucous membrane of the pelvis is rough, ulcerated, and studded with grayish-yellow nodules.

The left kidney contains no tubercles that are visible to the naked eye. It shows the gross changes of a chronic parenchymatous nephritis well advanced.

The urinary bladder contains a small amount of turbid urine. The mucosa is dark red, showing many ecchymotic spots. In the lower half there is a cluster of circular ulcers, varying from 2 mm. to 11 mm. in diameter, with slightly raised margins and grayish, finely nodular floors.

The prostate is converted into an aggregation of communicating cysts containing a purulent fluid. The largest of these cavities is 2 cm. in diameter. The walls are thick and fibrous and contain whitish nodules of variable size. Both seminal vesicles are enlarged and have thick walls containing small caseous nodules.

In the right epididymis is a hard nodule 1 cm. in diameter. Its cut surface is gray and exudes pus upon pressure. A very small gray nodule is found in the left epididymis. The testicles appear normal upon section.

The retroperitoneal lymphatic glands leading up from the pelvis are enlarged and contain caseous areas. The largest measures 2.5 cm. by 4 cm.

Histological Examination. The prostate shows only here and there a remnant of the gland tubules. Surrounding the abscess

cavities are thick masses of mature connective tissue containing caseous necrotic areas, some of which have calcified central zones. In places small masses of round-celled infiltrations are present. Giant cells are present, but are found only occasionally. The vascular walls are markedly thickened and tortuous; in places the lumen is almost obliterated. The peripheral muscle tissue is in some parts well preserved.

The walls of the seminal vesicles are thickly infiltrated with round cells, especially in the mucosa and submucosa, and contain numerous small isolated and conglomerate necrotic tubercles. The muscular layer is well preserved, though diffusely infiltrated with small round cells.

Histological evidence of tuberculosis is not found in sections of the vas deferens.

The left kidney shows only changes incident to parenchymatous nephritis, and no evidence of tuberculosis. The right kidney shows variable areas of necrosis and round cells in the neighborhood of abscess cavities. No appearance of sclerotic encapsulation or of calcification is met with.

The evidence upon which to base a conclusion that the genito-urinary tuberculosis in this case was primarily located in the prostate consists chiefly in the appearance of the lesion in that gland compared to other parts. Here we find an old infection, signified by great destruction of the gland and more by the surrounding connective-tissue increase, the thickening of the vessel walls, and the calcareous infiltration of certain necrotic areas. The disease in the right kidney is of the ascending type, with greatest involvement of the pelvis and pyramids, signifying infection from below. In hematogenous infection of this organ the process is first located at the bases of the pyramids and in the cortex, and, according to Weigert, tends to remain long localized. It must be said, however, that various and contradictory opinions are held concerning this fact, which will be discussed later.

CASE II.—W., a Russian, aged fifty-six years, and a laborer by occupation, was admitted to Cook County Hospital December 1, 1903, to the service of Dr. Amerson. It was impossible to obtain any history from him, except that he had been sick one and one-half years.

His skin was cold and clammy; the respirations were short, rapid, and labored. The heart was rapid, weak, and irregular, while a systolic blowing was heard about the area of the apex and was transmitted to the left axilla.

The lungs were negative. The liver was slightly enlarged, extending one finger's breadth below the costal margin. The spleen was not palpable. The abdomen was retracted. The external genitalia were normal, and the legs and feet were very cedematous.

On admission the patient's temperature was 98°. He experienced

much pain upon urination. He was very restless and slept but little. On the second day his temperature was 101°. Respirations remained high, and he coughed up much clear blood and seemed to suffer considerable pain. He died at 10 A.M., December 2d.

Autopsy. At the autopsy held by Dr. Le Count, the anatomical diagnosis was as follows: Tuberculosis of the prostate, seminal vesicles, and right epididymis; tuberculous peritonitis; generalized miliary tuberculosis of the lungs, pleura, kidneys, and spleen; ascites, hydropericardium, hydrothorax, and anasarca; dilatation of the mitral orifice; fibrous mural endocarditis; hypertrophy and dilatation of the heart; healed infarcts of the kidneys and spleen; cyanotic atrophy and cavernous angioma of the liver; "sago" spleen; moderate sclerosis of the coronaries.

The record of findings pertaining to our subject is as follows:

The prostate is moderately enlarged in both its lateral lobes. The external surface has nodular irregularities. It is the seat of a conglomerate caseous mass containing in the left lobe several abscesses of 1 mm. or 2 mm. in diameter.

The seminal vesicles are indurated and contain small caseous nodules in the walls. The right vas deferens close to the prostate is thickened and very firm. From here to the epididymis it appears to be normal. The ejaculatory duct is passable for a small probe. The right epididymis has a cyst in the globus major containing approximately half an ounce of clear, straw-colored fluid. The globus minor is one and one-half times its normal size and contains small, discrete, caseous nodules, which are softer than those in the prostate. The testicle contains no microscopic evidence of tuberculosis.

The bladder presents no gross changes.

The peritoneum, lungs, pleura, kidneys, and spleen contain miliary tubercles. No old or advanced tuberculous lesions are found in any of these organs.

Histological examination confirms the gross findings—advanced tuberculosis of the prostate, vesicles, and the epididymis and miliary tuberculosis of other organs.

The prostate shows large areas of discrete and conglomerate necrosis, with marked connective-tissue hyperplasia about them. There are numerous areas of round-celled infiltration arranged in groups. The gland tubules have largely disappeared. Those remaining show much desquamation of the epithelial lining. The vessel walls are thickened. No giant cells are found, but numerous tubercle bacilli were demonstrated in the tissue and in cover-glass preparations from contents of the seminal vesicles, the walls of which contain small caseous masses and much round-celled infiltration.

The epididymis shows only areas of round-celled infiltration and necrotic areas, with slight sclerosis, endoarteritis and periarteritis.

That the prostate in this case must have been the seat of a tuberculous process prior to its development in the epididymis and vesicles is signified by the vastly more advanced lesion, the larger areas of involvement, and the excess of surrounding sclerosis of the gland lesion. The general relation between prostatic and epididymis infection will be later discussed.

OCCURRENCE. That prostatic tuberculosis is not a rare disease, autopsy records amply demonstrate. Collinet found the prostate involved in 44 of 70 cases of genitourinary tuberculosis; Simmonds found it involved in 26 of 35 cases; Krzywicki in 14 out of 15 cases; Oppenheim in 18 of 25 cases; R. Koenig in 31 of 45 cases; Socin and Burckhardt in 44 out of 52 cases. Of the total of 242 cases, the prostate was found to be involved in 177, or 73 per cent. The relative uniformity of the various observations goes to prove the accuracy of the result. The prostate is involved in genitourinary tuberculosis, according to Socin and Burckhardt, with considerably greater frequency than any other single organ, except the kidney.

Opinions concerning the starting point of the disease in the genitourinary organs are various and contradictory. Autopsies are rare in the early stages, and late in the disease the process is likely to be so disseminated that it is difficult or impossible to designate the original focus. Rokitsky early stated that it begins, as a rule, in the epididymis and extends upward to the prostate, an opinion shared by Virchow and by Klebs. Cohnheim and Steinthal believe the infection always starts in the kidney and involves the genital organs secondarily. Weigert holds the opposite, believing the disease to begin in the genital organs and with relative frequency in the prostate. Simmonds found in his cases the epididymis most frequently involved; Oppenheim the seminal vesicles, and Krzywicki the prostate, and they respectively considered these the starting points of the genital infection. In all of his 14 cases Krzywicki found the oldest and most advanced lesions to be located in the prostate, and was the first to advance strongly the contention that genital infection begins there in the vast majority of cases. In 2 cases it alone showed any considerable lesion.

As it concerns the genital organs proper, Desnos believes that the prostate frequently presents the first localization of the infection. Lancereaux comes to the conclusion that it is always a descending process, and that the primary focus is to be sought for in the prostate or vesicles. From both clinical and pathologic-anatomical reasons, Monod and Terrillon believe that testicular tuberculosis is usually preceded by foci in the higher gland or vesicles. Kapsammer and Kocher express similar opinions. This view is also upheld by the investigations of R. Koenig, who asserts that the prostate plays a most important part in the development of tuberculosis of the testicles, and suggests that it may act as an intermediate station, where the bacilli develop with little or no reaction, awaiting

opportunity to progress along the vas to the testicles, and that even in apparently primary testicular tuberculosis, the prostate may first contain such undiscovered lesions.

Dimitresco says that the disease may begin in the prostate, seminal vesicles, or epididymis, the latter most frequently. Reynier takes a strong stand in favor of the epididymis, a view upheld upon clinical grounds by Senn, Murphy, and other observers.

Baumgarten attempted to solve the problem of extension in an experimental way. He injected tubercle bacilli into the urethra of rabbits and produced ulcerative urethritis, with invasion of the prostate, but no extension into either kidney or testicle, although some of the animals lived a year and a half after inoculation. Injected into the epididymis they invaded the prostate, but not the opposite testicle. He infers that dissemination does not take place in a direction opposite to the secretory flow; that the tubercle bacillus, having no power of locomotion, cannot progress against the current of a secretory fluid. From autopsy experience he believes that similar conditions obtain in man, a proposition which is disputed by F. König in discussing his paper.

Of great interest in this connection are also the experiments of Paladino-Blandini. He injected various organisms, both pathogenic and non-pathogenic, into the anterior urethra of guinea-pigs, and always found that some of them reached the epididymis after a variable period. The non-pathogenic forms disappeared again in a short time; the pathogenic kept their habitat somewhat longer, but finally disappeared, unless outside influences were brought to bear. Tubercle bacilli reached the epididymis after thirty hours in repeated experiments, and frequently also the testicle and the kidney. They did not produce specific inflammatory lesions unless trauma or circulatory disturbances were brought into play. The organisms were demonstrated both by microscopic examination and by direct inoculation experiments upon other animals.

All forms of urogenital tuberculosis are in the great majority of cases secondary to primary foci in some other part of the body, chiefly the lungs, or, as Heiberg says, the bones. Our question then concerns for the most part the starting point and mode of dissemination of a secondary tuberculous infection. It seems to be amply proven that any one of the genitourinary organs may be first involved, and that either an ascending or descending extension may take place. Of the genital organs, it seems to have been clearly demonstrated, and the opinion is largely supported, that the prostate presents the earliest localization in a large proportion of cases and plays an important part in dissemination.

From the clinical side, proof of this is scarcely possible. The prostate is deep-seated and inaccessible, while the epididymis lies freely exposed, and is hence more likely to have its pathological states discovered. Furthermore, small or even considerable lesions

in the prostate may be unaccompanied by symptoms; hence adequate investigation is often not made. From the pathological side, evidence of a convincing character points to first involvement of the prostate in many cases.

Though primary prostatic tuberculosis, in the sense that no other organ in the body presents an earlier manifestation of the disease, is an exceptional and relatively rare condition; it is, nevertheless, a well-established one, both from a clinical and pathological point of view. Socin reports 2 such cases. Möller found at autopsy miliary tubercles in the peritoneum and other parts with no advanced lesion, except that of a hazelnut-sized caseous mass in the prostate. Claude records a case in which, after death from acute colon bacillus peritonitis, no other tuberculous focus was found, even in the genito-urinary organs, aside from one in the prostate. Marwedel, Krzywicki, Conitzer, Kapsammer, and others report cases equally convincing.

ETIOLOGY. Tuberculosis of the prostate begins most frequently in early adult life, attaining its maximum frequency between the ages of twenty and forty years—during the period of greatest sexual activity—though no period of life is exempt. Exceptionally cases are met with in children and in old age. Marwedel observed one case in a man of sixty-three years; Hoffmann, one at sixty-eight years; and Socin, one at seventy-five years. Simmonds found three-fourths of 60 cases of genital tuberculosis between the ages of twenty and fifty years, and two cases in children of one and one-half and seven years, respectively.

As in all forms of tuberculosis, heredity plays an important part in that of the prostate. In 35 cases Desnos found tuberculosis in the antecedents of 16. Fetal implantation of the tubercle bacillus is, indeed, possible the organism awaiting an opportunity of development until some external influence exerts a harmful effect upon the prostate, making it a region of low resistance.

Similarly, in those cases developing as distinctly secondary to pulmonary or other tuberculous foci, external influences are of importance as exciting causes. Trauma, on account of the protected position of the gland, plays no important part, though several cases in the literature followed falls upon the buttocks. Those things are to be chiefly considered which tend to cause congestion and inflammation of the prostate, and most frequent among these is gonorrhoea. A large proportion of cases develop subsequent to such an infection. Englisch says that simple inflammatory processes in the tissues surrounding the prostate may play an important part. Urethral strictures, cystitis, excessive coitus, onanism, exposure to cold, infected sounds, and sound traumas are generally conceded as exciting causes. Still, a few cases develop without any such discoverable influence.

Obviously, the one etiological necessity is that the tubercle bacillus shall find its way into the gland. In what way does this take

place? Generally by direct implantation of tubercle bacilli from the blood or lymph stream, which acts as the carrier from distant parts. Jani made the interesting and important observation that tubercle bacilli are often found in the healthy prostates of those suffering from phthisis. He was able to demonstrate them in 4 out of 6 cases examined. Here they may rest until some of the influences noted above are brought into activity. Weigert had already called attention to the fact that in at least half of all pyæmic processes abscesses are to be found in the prostate. He believes, therefore, this gland is especially predisposed to the lodgement of organisms. Upon this ground Jani explains the numerous tubercle bacilli which he found in smears from prostatic fluid. In sections the organisms were found in the region of the gland tubules, between and beneath the epithelial cells, with the merest trace of tissue reaction about them.

It is also possible that bacilli may pass from the circulation through an intact kidney with the urine and be carried down to collect in the prostatic sinus, where the numerous ducts of the sieve-like floor of the urethra offer ample opportunity for lodgement and growth. That the kidney is passable by certain micro-organisms without itself becoming the seat of pathological changes has been shown by Gravitz and other observers.

Primary prostatic tuberculosis offers rather more difficulty to explanation than secondary. The blood stream is probably the chief mode of infection in these cases also. Pathological observation furnishes abundant evidence that the bacillus may pass through a mucous surface and produce no discoverable lesion. Note the frequency of infection in lymph glands draining exposed surfaces, especially the throat, lungs, and bronchi. From these glands the organism may find its way into the blood stream, without having produced any visible local lesion, and be lodged in the prostate—Weigert's "place of predilection."

Direct infection of the prostatic urethra by the use of bacillus bearing sounds or catheters is to be looked upon as a possible though certainly in this day a very rare mode of infection.

The possibility of infection through coitus has been much discussed and variously interpreted. Marwedel says it is not to be proven and that all evidence stands against it. Kapsammer is convinced that it does not occur. Excessive intercourse may indeed furnish the opportunity for latent germs to develop or for those in the blood to locate and grow, but this relation is to be sharply distinguished from a true cause—a direct infection from the tuberculous female genitalia. If infection did occur in such a way, it is reasonable to suppose that tuberculous lesions of the glans or urethra would precede the deeper localization and would be relatively much more frequent than the deeper disease.

Tschlenoff has recently investigated this subject fully. He observed a case of primary tuberculous ulceration of the penis, sup-

posedly of venereal origin. He was able to find but one other case in the literature. In neither case was the lesion proven by autopsy to be primary. He was able to collect a small number of reported cases of secondary tuberculous autoinfection of the penis, but they seem to be rare. Dobroklonsky, who is stated to have given the most attention to this subject, is only able to assert the possibility of infection by coitus.

Krecke attempted to explain the absence of peripheral lesions by the fact that the urinary stream would wash out bacilli from the urethra, but when they had once attained to the prostatic sinus conditions would be favorable to their development. If constantly washed away, how are they to reach the prostatic sinus? He compares it to the way in which tubercle bacilli reach the lung through the upper air passages; but the case is very different, for here they are carried by the air current and deposited directly upon the walls of the alveoli and smaller bronchi.

Schuchardt maintains not only that infection may occur from sexual intercourse, but that such infection is frequent, mixed with the ordinary venereal diseases. He cites several cases in support of his opinion, and suggests that the tubercle bacilli found in healthy prostates by Jani may be the result of mixed gonorrhoeal-tuberculous infection. One of his cases with acute posterior urethritis developed an abscess in the prostate, the pus from which showed gonococci and tubercle bacilli. The case resulted in recovery. No sufficient evidence is given of the previous absence of tuberculosis. Both his work and his conclusions are forcibly criticised by Kraske. Cornil and Babes found tubercle bacilli and gonococci in a case presenting only the signs and symptoms of gonorrhoea. Klebs reported a case where acute miliary tuberculosis developed after gonorrhoea, suggesting a mixed infection. But none of these cases carry convincing proof of infection by coitus.

As already stated, Baumgarten produced ulcerative urethritis with extension into the prostate by injecting rabbits' urethras with tubercle bacilli, while Hanau produced only the urethritis by the same methods applied to guinea-pigs. These experiments cannot be considered analogous to coitus, since the organisms were actually projected deep into the urethra and in large numbers. On the side of result, local urethral lesions were produced, which are almost unknown in man, except as late involvements by extension from the prostate or as autoinfections.

On the other hand we must consider the experiments of Paladino-Blandini as being of great importance in this relation. While he did not produce deep lesions, he demonstrated that tubercle bacilli may reach a deep location from being planted on the mucosa near the meatus. If then there occurs at the same time some harmful influence upon the sexual glands, such as excessive or prolonged physiological congestion, old gonorrhoeal infection or trauma, it

would seem to make direct infection from coitus a highly probable occurrence. This on the unproven supposition that similar conditions obtain in man.

Though infection by way of the urethra through sexual intercourse must be looked upon as a possibility, no sufficient evidence of its actual occurrence has yet been produced.

ANATOMY. As shown by the studies of Jani, in what may be called the prepathological stage of tuberculous infection of the prostate, the primary localization of tubercle bacilli in that organ is in the neighborhood of the gland tubules. Other studies of the early stages of the disease show that along the tubules first appears localized round-celled infiltration with progression to typical histological tubercles, which gradually enlarge, coalesce, and caseate. Tubules are compressed, obstructed, or dilated in different parts; the epithelium degenerates and becomes desquamated, filling the acini with granular detritus which may contain the bacilli. Caseous nodules appear in one or several places, in one or both lateral lobes, though very rarely in the middle lobe, and by a progressive involvement of tissue may come to include practically all the gland substance (Case II.). There is a great tendency to liquefaction and abscess formation, a fact often dependent upon secondary infection from bacteria inhabiting the urethra. Hence either "septic" or "cold" abscess may be present. When small, the latter may undoubtedly be absorbed with local scar formation. Calcification may take place in part (Case I.) or rarely *in toto*. Broca reports a case where almost the whole prostate was one calcareous mass. As rare conditions are to be noted cases reported by Marwedel and by Fuller, in which the whole gland was converted into a single large sequestrum.

In a few instances only has a pure miliary tuberculosis been observed in the prostate.

There is a tendency to early involvement of other parts of the genital apparatus, particularly the seminal vesicles and bladder, by the way of the mucous membranes. The former become the seat of isolated or diffuse caseous necrosis, following a round-celled infiltration and tubercle formation. Epithelium is desquamated; the cyst contents contain detritus, pus cells, and perhaps tubercle bacilli (Case II.). The bladder involvement first appears in the region of the urethral orifice and the trigone. In the early stages it is the seat of miliary tubercles, and later of more or less advanced ulcerative processes. The vas is usually involved by a tuberculous infiltration near the prostate, and if there is coexistent disease of the epididymis, suffers more or less throughout its whole extent. It may, however, remain free from discoverable lesions along most of its course, even with marked lesions in the epididymis and testicle.

Generalized miliary tuberculosis is not an infrequent ultimate result. Weichselbaum found a large vein of the plexus pudendalis

enclosed in a caseous mass by extension, with a rupture into the vein at one point as the source of such dissemination.

With the development of abscesses in the prostate come the more important complexities of the anatomical picture. While these are yet small they may break into the gland tubules and escape through the ducts into the urethra. If larger and progressive they come to the gland capsule, involve and ultimately destroy it and break into neighboring parts. The prostatic urethra is the most frequent site of such rupture; next come the rectum, the bladder, the bulbous urethra, and perineum. In a case reported by Vollimier and Le Dentu, the whole of the penis to within a centimetre of the glans was invaded by the abscess, not as a simple burrowing, however, but succeeding a tuberculous periurethritis produced by direct extension. A very rare result is rupture into the peritoneum, which was once observed by Socin.

Various and sometimes complex fistulæ are brought about by the rupture of abscesses from the prostate into the urethra, rectum, bladder, seminal vesicles or perineum, singly or in combination. Those passing between the urethra and rectum are relatively common. Toward the end the prostate may be entirely converted into a cavity communicating with the bladder and containing urine. Such conditions were observed by Marwedel, Conitzer, and Bond and Windel. The last-named case is particularly interesting from the fact that this cavity was as large as the bladder itself, with which it communicated by a small opening. Multiple fistulæ may open into the rectum or on the perineum.

In the early stages the volume of the prostate may not be much altered. As the disease becomes more advanced moderate enlargement is usually found, and a degree of nodular irregularity of the surface. Sometimes advanced caseation or abscess formation cause great increase in size. Reclus records a prostate measuring 64 mm. across, Lancereaux one five times the normal dimensions and Bacaloglu one three times the normal; but the rule is to have only moderate enlargement. Not infrequently, by reason of emptied abscesses, there may be actual decrease in the size of the gland.

SYMPTOMS AND DIAGNOSIS. If a tuberculous focus is situated deeply within the substance of the prostate, it may remain long without symptoms. Even up to the time of death may this be true. In Möller's case, in spite of a large caseous nodule in the gland, there was absolutely no history of urinary or genital trouble and a perfectly normal urine. Nor in those cases with extension to surrounding parts is the symptomatology of such a definite form as to make diagnosis always possible. Marwedel expresses the belief that more than a third of the cases run a symptomless course and that in many more the diagnosis is never made. Careful physical and bacteriological examination would no doubt do much to clear up a large proportion of these cases with slight symptoms.

I have recently observed a case of advanced disease in the prostate and one seminal vesicle, associated with tuberculosis of the epididymis, which gave absolutely no clinical symptoms. Rectal palpation left no doubt of the diagnosis.

Subjective symptoms usually develop sooner or later, often quite suddenly as the result of abuse, exposure or venereal infection, and are frequently of a most marked and troublesome character.

The most constant of these are disturbances of urination, at first slight, growing gradually in severity. There is frequency, which is greater by day than by night, pain or burning in the perineum and penis, posturination tenesmus and a feeling as if the bladder had not been fully emptied. The urine flows slowly from partial obstruction due to swelling of the gland. The symptoms often resemble closely those of the ordinary form of cystitis colli or catarrhal prostatitis with irritable bladder. Caspar makes the significant remark that the distinguishing feature between simple and tuberculous infection lies in the response to treatment. What relieves the simple forms only makes tuberculous worse. At times a constant call to empty the bladder and pain rob the patient of sleep and make him miserable indeed. Imperious call to urinate, with sharp pains radiating into the glans, usually signify extension to the bladder, and may be of such a character as to strongly suggest stone.

Acute retention may develop at any time from swelling of the prostate, or permanent obstruction render catheterization necessary for long periods. With advancing destruction the sphincters may be destroyed and permanent incontinence develop. Where there is a large abscess cavity communicating with the urethra, post-urination dribbling is likely to be present. Pressure upon the perineum may express the residue, as in one of Kapsammer's cases.

Chronic constipation is usually present, and pain in the rectum not infrequently occurs at stool. This may be slight or severe. Late in the disease fistulous tracts leading to the rectum or the perineum result in discharges of urine and pus by these routes.

Quite apart from urination and defecation, there is often a feeling of indefinite discomfort, pressure or actual pain in the perineum and rectum, which is increased by motion, sitting, or local pressure. It may be of great severity and long duration. Von Frisch tells of a patient who could neither sit nor lie down for weeks, using an apparatus for suspension in a standing posture, and where heroic doses of morphine failed to give relief; and of another who suffered greatly and constantly for some days after a rectal examination. Such severe pain is observed only when abscess is present.

To hematuria has been ascribed a more or less important place in the symptomatology of prostatic tuberculosis by most observers. Guyon, Socin and others say that it has no essential significance. Certainly it is rare as an initial symptom, though this has been observed by Gaudier and others. As a rule only a few drops of

blood are seen at the beginning or end of urination; more rarely it is discharged by the urethra between times. Exceptionally it may be discharged with the urine in large amounts. Clots in the bladder led to acute retention in one of Marwedel's cases where the bleeding was severe and prolonged. Reliquet records a case of veritable urethrorrhagia where pure blood followed urination. In whatever form hæmaturia occurs it signifies ulcerative processes communicating with the urethra or in the bladder. If continuing between periods of micturition it comes from ulcers in the deep urethra.

Frequent seminal emissions are observed in not a few cases. They are sometimes painful. There may be a few drops of blood tinging the discharge, and this may come from either the vesicle proper or be mixed with the semen in its passage through the prostatic urethra. Sexual power is generally well preserved, even when abscesses and fistulæ are present. In one of Kapsammer's cases there was a prostatic abscess with openings both to the rectum and the perineum and still no interference with ejaculation, urination or defecation. Seminal discharges may reach the rectum or bladder through fistulous tracts, events which are recorded by several observers, and in spite of this coitus may be carried out with normal sensation.

Urethral discharge is often present. This is sometimes a thin mucous substance containing granular detritus and a few pus cells, which Englisch has shown may occur in tuberculous individuals as a result of degenerative changes in the urethral mucosa without local infection. At other times it is purulent or composed of broken-down caseous material and signifies an abscess cavity communicating with the urethra or ulceration in the urethra itself. There may be a constant slight flow, though the rule is to have a few drops appear at the meatus at the end of micturition, after defecation or as a result of pressure upon the prostate from the rectum. Should a discharge appear after a suspicious coitus, it may simulate a gonorrhœal infection and be so interpreted by the patient. Marwedel and Kapsammer each report a case where such discharge, appearing fourteen days after exposure, marked the first symptoms of the disease. The physical character of the pus and the absence of the gonococcus are the distinguishing characteristics and a diagnosis is rendered certain by the finding of the tubercle bacillus, which systematic examination of the expressed prostatic fluid rarely fails to do.

The diagnosis of tuberculosis of the prostate usually cannot be made from symptoms alone. To a careful review of such as are recorded above, with the general symptoms of tuberculous infection, must be added a painstaking physical examination, which will rarely leave the clinician in doubt except in incipient primary cases. When the disease is well advanced, when there is extension to other parts, and especially when fistulæ are present, its recognition

becomes simple enough unless old uncured venereal infections complicate the local condition.

Passing of the catheter or sound reveals painful obstruction in the prostatic urethra. In the early stages this is due to swelling of the gland, later to ulcerative processes. When the latter become severe it may be impossible to enter the bladder with an instrument of ordinary form on account of the tip engaging in pockets. A woven catheter of the Mercier type may pass readily enough, though with instruments of whatever form it may be impossible to free the tip from ulcer margins or cavities into which it finds its way. Where the prostate is converted into a cyst or a series of large communicating cysts it is rarely possible to complete the introduction and false passages are readily made through the friable tissue. Pain is often severe. In a case I have recently examined it was practically impossible to introduce a small soft-rubber catheter on this account, even after 4 per cent. cocaineization.

The rectal examination is one of the most important procedures. Conitzer quotes Guyon as saying: "It is, so to speak, quite as necessary to frequently palpate the prostate in those who suffer from diseases of the urinary apparatus as to examine the heart in rheumatism." The gland is, as a rule, moderately enlarged, the lobes of unequal size and the surface marked by nodular irregularities, "feeling as if grains of lead were covered with an elastic parenchyma." (Forgue). Diffuse tenderness may be present, but more important are localized tender spots. When abscess forms tender fluctuating projections may be felt; when empty, they leave pit-like depressions. Tender swellings on the prostate, developing chronically and without discoverable cause of a venereal nature, are nearly always tuberculous. The finding of fistulous openings into the rectum is frequent in late cases. They may usually be felt by reason of slightly indurated margins and fast adhesions between the rectum and prostate about their openings. If brought into view by the proctoscope they may sometimes be seen to discharge urine. When the seminal vesicles are involved they are enlarged, tender and resistant, "as if filled out with wax." (Marwedel.)

The condition of the urine will vary greatly according to whether or not and to what extent the bladder is involved. It may remain entirely normal, as in Möller's case. The reaction remains acid, even when much pus is present, and a few blood cells are frequently found in the sediment. Acid urine containing pus from the bladder is to a certain extent characteristic, the acidity often persisting in spite of catheter or other secondary infection. Tubercle bacilli in the urine are relative to the destructiveness of the process. If they are not found it is no argument against an otherwise confirmed diagnosis.

When it is possible to render the bladder contents clear enough for a cystoscopic examination, this may be of great value. It not

only tells the condition of the bladder but the stage of advance of the disease, miliary tubercles representing an early, ulceration a later stage. It also enables one to recognize extension into the upper urinary passages. The examination is likely to be very painful. For this reason von Frisch discards it entirely for a majority of cases. The endoscope shows a congested prostatic urethra, ulcers, swollen calliculus seminalis, or fistulous openings on the urethral floor.

In the early stages, where the prostate is alone or chiefly involved, systematic expression of the prostatic fluid and bacteriological examination should always be resorted to in the hope of confirming a suspected diagnosis by the finding of tubercle bacilli.

COURSE AND PROGNOSIS. Tuberculosis of the prostate is always to be looked upon as a grave disease. The course will be rapid or slow according to whether the general health, strength and habits of the patient are good and whether the disease is local or only a part of a diffuse infection. A limited involvement in a strong individual offers the best prognosis. The general tendency is to progressive involvement of other parts of the genitourinary apparatus, abscess and fistula formation, and death from sepsis, uræmia or generalized tuberculosis.

The disease may, however, remain long localized and latent. Mitscherlich cites a case that became active as the result of a gonorrhoeal infection after sixteen years' standing. A case cited by Berand and Robin remained stationary for six years, and other observers record cases which remain for a long time quiescent and benign.

Spontaneous healing occurs in a minority of cases. Small caseous areas may suppurate and discharge through the urethra and heal by cicatrization; they may become encapsulated and latent or they may undergo calcification and encapsulation. Von Frisch states that he has seen two cases recover even after the bladder had become involved. Even when fistula formation and extensive complications are present, if no extension to the kidney has occurred, healing may take place spontaneously or as the result of operative intervention. Rectal fistulæ, and especially rectovesicular fistulæ, are likely to give rise to septic infection. They are not, however, to be looked upon as hopeless.

Supposed healing is to be accepted with reserve; recurrence is likely to occur. Klebs makes the statement that the gland once infected very seldom becomes entirely free. The earlier the diagnosis is made and the more strictly localized the process, the better are the results of treatment, hence the better prognosis.

TREATMENT. Tuberculosis of the prostate is amenable to surgical treatment in a certain small proportion of cases. Obviously it is only applicable when the disease is localized and limited to the genital apparatus, when tuberculosis of the lungs or other parts of the body is absent or in a latent state, and when the general condi-

tion of the patient is such as not to contraindicate operative procedures. Tuberculous abscess in the prostate should always be opened through the perineum in time at least to prevent its rupture into the rectum, which endangers the genital tract to secondary infection from fecal matter.

Marwedel says that abscess and fistula formation give the first indication for surgical interference, a course which seems to have been adhered to in the great majority of instances. He suggests, however, that it is not apparent why, when one has the opportunity to diagnose a prostatic tuberculosis early, when there is no general genitourinary or serious pulmonary tuberculosis, he should not directly attack the focus and attempt to cure the disease by removing it. In his recent work Socin expresses himself rather more strongly upon this point and advises surgical removal whenever the disease is limited and the patient's general condition is good, exactly as one would proceed in the case of tuberculous lymph nodes. Sarda, Fourgue and a few others express themselves in a manner somewhat similar, but generally advise great caution in the selection of cases for operation unless this is forcibly indicated by abscess and fistula or distressing symptoms.

Bryson discards surgery altogether except as a palliative measure in the late stages, for the relief of pain. In a few cases where the disease is well advanced, it seems as if operative interference had sometimes caused a more rapid dissemination than might otherwise have been expected. This is probably dependent more upon general than upon local conditions. Marwedel calls attention to cases in old men or in those already wasted by the disease and advises great caution in the use of the curette upon such people, even when symptoms calling for relief are of a severe sort. Young has recently reviewed the subject of operation from the standpoint of the seminal vesicles. From the good effect upon the higher process shown by removing an involved testicle, he is inclined to abstain from going directly into the vesicle and to rely first, at least, upon the minor operation. He expresses grave doubt as to the advisability of directly attacking the vesicles under any circumstances.

The logic of surgery would seem to lead to the conclusion of operation when the disease is sufficiently limited and seems to offer a fair prospect of radical removal. Recent improvements in the technique of prostatic surgery and its brilliant results also argue to this end. The number of operated cases on record is not yet large. Though operation as a rule has been undertaken relatively late in the disease, after the development of abscess and fistula, the results have been generally excellent. Cures have not been obtained in all cases, though a fair proportion have had that fortunate outcome, and those succumbing ultimately to the infection have nearly always received a great measure of relief from distressing subjective symptoms. If operation is to be ultimately necessary to afford such relief, it would

better be undertaken while the patient's general strength lends him a good degree of recuperative power and offers hope of cure.

Marwedel, Dittel, Sarda, Gaudier, Socin and others report cases of perfect cure. In some of the cases the disease was far advanced and the operation extensive. Socin removed not only the diseased prostatic tissue, but the seminal vesicles, part of the urethral floor and one testicle as well. Recovery is often rather prolonged and secondary operation is sometimes necessary to secure closure of troublesome fistulæ. Dittel, however, had a good recovery in one case after three weeks, without fistula or subjective symptoms remaining.

It is generally agreed that the best method of reaching the prostate for the removal of tuberculous foci is through a transverse, curved perineal incision. Operations for the opening of abscess have been carried out by both rectal and urethral routes, but these have been long since entirely abandoned. The perineal route brings the gland into view, can be rendered aseptic and is the most favorable place for fistula should this remain. When fistulæ are already present they should be slit up, scraped out with a sharp curette or excised, and followed to the prostate. Tuberculous foci in the gland are removed by the sharp spoon, the wound either packed with iodoform gauze and left open or sutured with a small gauze drain. Fistulæ leading to the rectum are opened, with division of the sphincter muscles if necessary. It is important to remove all that is possible of the tuberculous tissue. Should the urethra be opened, it should be sutured if possible. Socin and Marwedel both saw perfect recovery after such an accident, though temporary fistulæ resulted.

When bladder symptoms are severe, suprapubic cystotomy is advisable in the opinions of Mayer and Hänel, Conitzer, and Socin, and should accompany operative procedures attacking the prostate through the perineum.

Desnos exposed the prostate by a perineal incision and injected a solution of chloride of zinc into the parenchyma of the tuberculous gland and obtained sclerotic atrophy in from four to six weeks. His report was made too early, however, to be able to judge with accuracy of the ultimate results of this treatment. Parenchymatous injections of iodoform emulsion have been recommended, but the method has received very little support. Sarda and others condemn all parenchymatous injections on account of the possibility of serious accidents.

Various forms of local treatment other than operative have been tried with variable success. Lane claims to have cured a case after repeated operation had failed to give relief, by injecting an emulsion of sulphur in glycerin into a complex system of fistulous tracts, one of which opened into the rectum.

Berkley Hill is a warm exponent of injections of iodoform emul-

sion into the prostatic urethra and bladder, advising previous cocaine-ization or even general anæsthesia if pain is severe. Most other observers see no benefit from its use. Merwedel prefers a 2 per cent. solution of balsam of Peru, from which he saw good results. The best results of local treatment seem to have come from corrosive sublimate in solutions of 1:6000 to 1:2000, used as an instillation or irrigation. Silver nitrate is invariably harmful. In the beginning of the disease Marwedel observed good effects from cold applied per rectum.

Whatever form of local treatment requiring instrumentation applied through the urethra is capable of doing harm and is to be used with great care and foresight and graded to the patient's tolerance. Thompson long ago called attention to this, advising the avoidance of the catheter and all irritants. Desnos discards such forms of local treatment entirely. So long as the disease produces only the symptoms of a local catarrh, it should be treated by general measures only.

The general treatment is that of tuberculosis in other parts of the body: good diet, out-door life and whatever tends to improve the general health of the patient. Guaiacol, creosote carbonate and such things may be useful.

In a certain sense we may speak of a real prophylaxis against genital tuberculosis. Any tuberculous individual who is likely to be exposed to a gonorrhœal infection should be warned against the excess of danger that lies in this disease by reason of his condition. If such venereal infection occurs it should be treated with the utmost care and the patient put to bed in the mean time. He should be warned also against the possible results of sexual excesses. If a genital localization of his tuberculous infection has taken place, he should be advised to secure the greatest possible physiological and physical rest for his genitourinary system, as he would for any other system involved in a like infection.

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A RESUME OF THE ISSUES CONCERNED IN THE DIAGNOSIS AND TREATMENT OF RENAL TUBERCULOSIS.*

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To what extent renal tuberculosis has risen from obscurity may be judged from what follows. In the period of 1867 to 1895 at von Bergmann's clinic, of 55 cases operated upon for kidney diseases, as reported by Lotheisen,¹ but 2 cases of renal tuberculosis were encountered. In 1902 von Schmieden² collected 2100 cases of renal disease, representing 201 nephrectomies for tuberculosis, among which were 22 of Schede's own cases operated in the interval of 1886 to 1892. This great disparity in the number of the cases of the two operators is at first accounted for by the recognition of the bacillus tuberculosis, and eventually by a more liberal use of the cystoscope in aiding the early diagnosis of this affection.

The most commonly encountered subjective clinical symptoms of renal tuberculosis are *pyuria*, *polyuria*, *pain*, and *hematuria*, together with some slight constitutional disturbance. A moment's consideration shows that this symptom-complex is peculiar to other diseased organs of the genitourinary tract, and yet there is something distinctive about each symptom that attracts attention to the possible existence of tuberculosis. First and foremost, it is an axiom that painless pyuria in adults between twenty and forty, which is associated with symptoms of bladder irritability, and which does not yield to ordinary treatment, is, in all likelihood, tuberculosis of the bladder dependent upon renal lesions; and if, furthermore,

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